

**PCT**WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau

## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>6</sup> : <b>A61K 7/16</b>	<b>A1</b>	(11) International Publication Number: <b>WO 95/34275</b> (43) International Publication Date: 21 December 1995 (21.12.95)
<p>(21) International Application Number: PCT/EP95/02308</p> <p>(22) International Filing Date: 16 June 1995 (16.06.95)</p> <p>(30) Priority Data: 9412048.2 16 June 1994 (16.06.94) GB</p> <p>(71) Applicant (for all designated States except US): THE BOOTS COMPANY PLC [GB/GB]; 1 Thane Road West, Nottingham NG2 3AA (GB).</p> <p>(72) Inventors; and (75) Inventors/Applicants (for US only): HAYWOOD, Julia [GB/GB]; The Boots Company plc, 1 Thane Road West, Nottingham NG2 3AA (GB). PULLEN, John, Hamilton [GB/GB]; The Boots Company plc, 1 Thane Road West, Nottingham NG2 3AA (GB).</p> <p>(74) Agent: KIRK, Martin, John; The Boots Company plc, Group Patents Dept., 10th floor, Newland House, 49 Mount Street, Nottingham NG2 3AA (GB).</p>		<p>(81) Designated States: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT, UA, UG, US, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), ARIPO patent (KE, MW, SD, SZ, UG).</p> <p><b>Published</b> <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p>
<p>(54) Title: ORAL HYGIENE COMPOSITION</p> <p>(57) Abstract</p> <p>An oral hygiene composition, especially a toothwhitening composition, comprises a silica abrasive and a particulate cellulose cleaning/polishing agent (particle size less than 50 <math>\mu</math>m). Also disclosed are oral hygiene compositions comprising one or more ingredients to enhance cleaning action selected from: alkali metal bicarbonate, alkali metal orthophosphate, alkali metal citrate and any compatible mixtures thereof, preferably in combination with a cellulose cleaning/polishing agent. Preferably the cellulose cleaning agent is powdered cellulose. The use of particulate cellulose as the sole abrasive to remove/prevent build-up of stains on teeth is also disclosed.</p>		

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	GB	United Kingdom	MR	Mauritania
AU	Australia	GE	Georgia	MW	Malawi
BB	Barbados	GN	Guinea	NE	Niger
BE	Belgium	GR	Greece	NL	Netherlands
BF	Burkina Faso	HU	Hungary	NO	Norway
BG	Bulgaria	IE	Ireland	NZ	New Zealand
BJ	Benin	IT	Italy	PL	Poland
BR	Brazil	JP	Japan	PT	Portugal
BY	Belarus	KE	Kenya	RO	Romania
CA	Canada	KG	Kyrgyzstan	RU	Russian Federation
CF	Central African Republic	KP	Democratic People's Republic of Korea	SD	Sudan
CG	Congo	KR	Republic of Korea	SE	Sweden
CH	Switzerland	KZ	Kazakhstan	SI	Slovenia
CI	Côte d'Ivoire	LI	Liechtenstein	SK	Slovakia
CM	Cameroon	LK	Sri Lanka	SN	Senegal
CN	China	LU	Luxembourg	TD	Chad
CS	Czechoslovakia	LV	Latvia	TG	Togo
CZ	Czech Republic	MC	Monaco	TJ	Tajikistan
DE	Germany	MD	Republic of Moldova	TT	Trinidad and Tobago
DK	Denmark	MG	Madagascar	UA	Ukraine
ES	Spain	ML	Mali	US	United States of America
FI	Finland	MN	Mongolia	UZ	Uzbekistan
FR	France			VN	Viet Nam
GA	Gabon				

### Oral hygiene composition

The present invention relates to oral hygiene compositions, especially toothwhitening compositions such as toothwhitening toothpastes. There is also provided inter alia the use of such compositions in the  
5 treatment and/or prevention of dental caries and/or gingivitis and in the cleansing of the buccal cavity for cosmetic purposes.

The term 'oral hygiene composition' as used herein denotes a formulation for use in any form of oral hygiene or dental treatment and includes inter alia dentifrices, mouthwashes, toothpastes, toothgels,  
10 toothpowders, lozenges and denture cleansing formulations and/or coatings for coating or impregnating dental accessories such as dental floss, toothbrush bristles and tooth picks.

The use of abrasive materials as cleansing and/or polishing agents in oral hygiene compositions is well known in the art.

15 For example GB-A-1186706 (Unilever) describes the use of particulate silica gel having an average particle diameter of from 2 to 20 microns as a polishing and cleansing agent in a dentifrice.

US-A-3538230 (Pader) describes the use of silica xerogels having an average particle size of from about 2 to about 20 microns as polishing  
20 and cleansing agents in a dentifrice.

However, use of high levels of such silica-type abrasives may risk causing damage to the teeth by wearing away the vital enamel layer and also dentine that may, for example, be exposed due to gum recession. There is thus a fine balance between achieving effective abrasive action to

CONFIRMATION COPY

clean and/or whiten/polish the teeth on the one hand without causing damage on the other hand.

FR 2625676 (Pharmascience) discloses a toothpaste to eliminate dental plaque and the staining of teeth characterised in that it includes as  
5 abrasive cleaning agent, a mixture of mineral abrasive agents having particle sizes less than  $20\mu\text{m}$  and an abrasive capacity less than 50, and a natural or synthetic organic polymer insoluble in water, having no gelling capacity and a particle size of between  $50\mu\text{m}$  and  $100\mu\text{m}$ . It is stated that the polymer is preferably a hydrophilic polymer, in particular cellulose or  
10 cellulose derivatives. The example given for such an organic polymer is the known product 'Avicel PH105' (RTM), which is a microcrystalline cellulose.

Microcrystalline cellulose is produced from grinding, cleaning and bleaching a source of cellulose (eg wood) and then hydrolysing the treated  
15 cellulose with acid (eg HCl), followed by spray drying. The result is a fractionated cellulose product with a high degree of crystallinity and a small amount of amorphous material. The treatment with acid produces a material which is partially hydrolysed with a low degree of polymerisation. Microcrystalline cellulose is to be contrasted with powdered cellulose,  
20 which is the material obtained simply after grinding, cleaning and bleaching the cellulose source. The absence of acid hydrolysis and spray drying in the production of powdered cellulose results in a less processed material of different particle shape, which comprises more amorphous material, has a higher degree of polymerisation and is cheaper to produce than  
25 microcrystalline cellulose.

The teaching of FR-2625676 as evidenced by the examples and the clearly envisages use of a microcrystalline cellulose ingredient of particle size  $50\text{-}100\mu\text{m}$  as the organic polymer abrasive. This document also

states that it is impossible to obtain advantageous results with the use of only a single abrasive agent.

US-A-5158764 (Degussa) describes a cellulose powder with a particle size of from 1 to 300 microns which may be used as a polishing agent in a dentifrice. The document gives examples of toothpaste formulations comprising a cellulose powder (particle size 40-150 $\mu$ m) in combination with a silica material available under the trade name "Aerosil" in an amount of up to 3% by weight. The silica is "pyrogenically produced" and so acts as a thickener rather than an abrasive. The document states that the cellulose material may be used to remove/eliminate plaque formations on the teeth.

Surprisingly, it has now been found in one aspect of the present invention, contrary to the teaching of the prior art, particulate cellulose may also be used to remove stains from the teeth (as distinguished from plaque), may be used to reduce and/or prevent the build-up of such stains, and is effective when used as the sole abrasive ingredient.

The term "stain" as used herein means an extrinsic stain in the form of a coloured deposit on the teeth. Such stains may be caused, for example, by smoking, eating and drinking things such as tea, coffee and red wine, or by cationic antibacterials and chromogenic bacteria. Stain does not appear to have health threatening consequences and its removable is desirable for cosmetic reasons only. In contrast with stains, dental plaque is a complex mass of bacteria that forms on teeth and is the etiological factor responsible for caries and periodontal diseases. Plaque is soft and can generally be removed fairly easily, for example by brushing with water. Stains on the other hand are absorbed onto the hard pellicle on teeth and are much more difficult to remove.

Accordingly, one aspect of the present invention provides the use of an oral hygiene composition comprising a particulate cellulose cleaning/polishing agent as the sole abrasive ingredient, to remove stains from the teeth and/or to reduce and/or prevent the build-up of stains on  
5 the teeth.

Suitably, the cellulose cleansing and/or polishing agent has a particle size of from about 1  $\mu\text{m}$  to 350  $\mu\text{m}$ , suitably from about 10  $\mu\text{m}$  to about 100  $\mu\text{m}$ , more suitably from about 20  $\mu\text{m}$  to about 70  $\mu\text{m}$ . A preferred cellulose cleaning/polishing agent comprises a high percentage  
10 of  $\alpha$ -cellulose comprising 1,4- $\beta$ -glycosidically linked D-glucose molecules with a degree of polymerisation of about 500 or more.

Suitably the particulate cellulose may comprise the powdered and/or microcrystalline type. More suitably, the particulate cellulose is highly purified powdered cellulose such as that available under the trade names  
15 'Elcema' from Degussa AG and 'Vitacel' from Allchem International.

The term "particulate cellulose cleaning/polishing agent" as used herein denotes a material which is capable of remaining substantially particulate in the oral hygiene composition on storage and in particular it is to be distinguished from cellulose gums and derivatives thereof. The term  
20 "powdered cellulose" as used herein denotes a material which is prepared as described above and in particular is to be distinguished from the more processed microcrystalline cellulose.

Suitably, the cellulose cleaning/polishing agent comprises from about 0.5% to about 25% by weight, preferably from about 1% to about  
25 10%, suitably about 5% by weight of the oral hygiene composition.

It has also been found that combinations of a particulate cellulose cleansing/polishing agent of a smaller size (less than 50  $\mu\text{m}$ ) than

previously known with various other abrasive agents provide surprisingly effective cleaning action without causing damage to tooth enamel.

According to a further aspect of the present invention broadly there is provided an oral hygiene composition comprising a combination of a  
5 particulate cellulose cleaning/polishing agent having a particle size of less than 50  $\mu\text{m}$  together with a non-cellulose abrasive. In particular the cellulose particle size may be less than about 40  $\mu\text{m}$ , for example about 35  $\mu\text{m}$ .

Suitably the powdered cellulose and non-cellulose materials are  
10 present in a ratio from about 5:1 to 1:5 by weight.

Suitably, the non-cellulose abrasive is selected from: silica, alumina, insoluble metaphosphates, calcium carbonate, dicalcium phosphate (in dihydrate and anhydrous forms), calcium pyrophosphate, natural and synthetic clays, and particulate thermosetting polymerised  
15 resins selected from melamine-ureas, melamine-formaldehydes, urea-formaldehydes, melamine-urea-formaldehydes, cross-linked epoxides, melamines, phenolics, cross-linked polyesters and any compatible mixtures thereof.

Suitably, the composition comprises from about 0.1% to about 25%  
20 by weight, preferably from about 1% to about 15%, suitably about 5% by weight of the non-cellulose abrasive. Suitably, about 98% or more of the non-cellulose abrasive has a particle size of less than about 45  $\mu\text{m}$ , optionally between about 25  $\mu\text{m}$  and about 45  $\mu\text{m}$ .

Preferably, the non-cellulose abrasive is a particulate silica abrasive.  
25 Suitable silica abrasives include the hydrated silicas, particularly those available under the trade names 'Sident' from Degussa AG, 'Zeodent' from J M Huber Corporation and 'Syloblanc' from W R Grace.

Unexpectedly, it has been found that certain alkali metal salts enhance the cleaning and/or polishing action of oral hygiene compositions, in particular those comprising a cellulose abrasive.

Therefore, in a further aspect of the present invention broadly there is provided an oral hygiene composition comprising a particulate cellulose cleaning/polishing agent and an agent to provide an enhanced cleaning/polishing action selected from one or more of: an alkali metal bicarbonate, an alkali metal orthophosphate, an alkali metal citrate and any compatible mixtures thereof. In such a composition the particulate cellulose abrasive may comprise powdered cellulose and/or microcrystalline cellulose. The cellulose abrasive may be the sole abrasive or be used in combination with other non-cellulose abrasives. Such compositions are suitable for removing stains and/or plaque. The preferred amounts and particle sizes of the particulate cellulose in such compositions are as given for the compositions described above.

Preferably, the composition further comprises an alkali metal bicarbonate, suitably sodium bicarbonate. Such a bicarbonate may be included in an amount of from about 0.1% to about 30%, suitably from about 1% to about 25%, more suitably from about 2% to about 10%, most suitably from about 2% to about 7% by weight of the oral hygiene composition, for example about 5% by weight. Inclusion of a bicarbonate provides an enhanced cleaning action.

Preferably, the composition further comprises an alkali metal orthophosphate, suitably monosodium phosphate, disodium phosphate and/or trisodium phosphate. Such phosphates may be included in an amount of from about 0.1% to about 10%, suitably from about 0.5% to about 5%, more suitably from about 0.5% to about 3% by weight, for example about 1% by weight of the oral hygiene composition. The presence of phosphates enhances cleaning action further.



It will be appreciated that where an alkali metal bicarbonate and an alkali metal orthophosphate are present together in the composition, the species selected must be compatible with one another. Strongly acidic species should not normally be present when bicarbonate is present, as  
5 otherwise an acid/base reaction may take place liberating carbon dioxide. It has been found that the combination of sodium bicarbonate, tripotassium citrate and trisodium orthophosphate is stable in use.

Preferably the composition further comprises an alkali metal citrate such as disodium citrate or tripotassium citrate. Such a salt gives a  
10 toothwhitening preparation of enhanced efficacy. Disodium citrate or tripotassium citrate are suitably used in amounts of about 0.1% to about 5%, preferably about 0.5% to about 3% by weight of the oral hygiene composition.

In yet a further aspect of the present invention broadly there is  
15 provided use of an agent to enhance the cleaning/polishing action of an oral hygiene composition, the agent being selected from: an alkali metal bicarbonate, an alkali metal orthophosphate, an alkali metal citrate and any compatible mixtures thereof.

The oral hygiene compositions described herein may be formulated  
20 for use in any form of interdental or periodontal treatment and may be in the form, for example, of a dentifrice or toothpowder.

Such compositions may, as appropriate, contain conventional materials such as, for example, humectants, surfactants, gelling agents, further abrasives, fluoride sources, desensitising agents, flavourings,  
25 colourings, sweeteners, preservatives, structuring agents, bactericides, anti-tartar agents and anti-plaque agents.

Suitable humectants for use in dentifrice compositions include polyhydric alcohols such as xylitol, sorbitol, glycerol, propylene glycol and polyethylene glycols. Mixtures of glycerol and sorbitol are particularly effective. A humectant helps to prevent dentifrice compositions from  
5 hardening on exposure to air, and may also provide a moist feel, smooth texture, flowability, and a desirable sweetness in the mouth. Suitably, such humectants may comprise up to about 85%, preferably up to about 60% by weight of the oral hygiene composition.

Suitable surfactants for use in dentifrices, mouthwashes etc. are  
10 usually water-soluble organic compounds, and may be anionic, nonionic, cationic or amphoteric species. The surfactant used should preferably be reasonably stable, and able to produce a foam in use.

Anionic surfactants include the water-soluble salts of C<sub>10-18</sub> alkyl sulphates (e.g. sodium lauryl sulphates), water soluble salts of C<sub>10-18</sub>  
15 ethoxylated alkyl sulphates, water soluble salts of C<sub>10-18</sub> alkyl sarcosinates, the water-soluble salts of sulfonated monoglycerides of C<sub>10-18</sub> fatty acids (e.g. sodium coconut monoglyceride sulfonates), alkyl aryl sulfonates (e.g. sodium dodecyl benzene sulfonate) and sodium salts of the coconut fatty acid amide of N-methyltaurine.

20 Nonionic surfactants suitable for use in oral compositions include the products of the condensation of alkylene oxide groups with aliphatic or alkylaromatic species, and may be for example, polyethylene oxide condensates of alkyl phenols, ethylene oxide/propylene oxide copolymers (available from BASF Wyandotte Chemical Corporation under the trade  
25 name 'Pluronic'), ethylene oxide/ethylene diamine copolymers, ethylene oxide condensates of aliphatic alcohols, long chain tertiary amine oxides, long chain tertiary phosphine oxides, long chain dialkyl sulfoxides and mixtures thereof. Alternatives include ethoxylated sorbitan esters such as those available from ICI under the trade name "Tween".

Cationic surfactants are generally quaternary ammonium compounds having one C<sub>8-18</sub> alkyl chain and include, for example, lauryl trimethylammonium chloride, cetyl trimethylammonium bromide, cetyl pyridinium chloride, di-isobutylphenoxyethoxyethyl dimethylbenzyl-  
5 ammonium chloride, coconut alkyltrimethylammonium nitrite and cetyl pyridinium fluoride. Also useful are benzyl ammonium chloride, benzyl dimethyl stearyl ammonium chloride, and tertiary amines having one C<sub>1-18</sub> hydrocarbon group and two (poly)oxyethylene groups.

Amphoteric surfactants are generally aliphatic secondary and  
10 tertiary amines comprising aliphatic species which may be branched or unbranched, and in which one of the aliphatic species is a C<sub>8-18</sub> species and the other contains an anionic hydrophilic group, for example, sulfonate, carboxylate, sulphate, phosphonate or phosphate. Examples of quaternary ammonium compounds are the quaternized imidazole  
15 derivatives available under the trade name 'Miranol' from the Miranol Chemical Company.

Suitably, the surfactant is included in an amount up to about 20%, preferably up to about 10% by weight of the oral hygiene composition.

Structuring agents may be required in, for example, dentifrices and  
20 gums to provide desirable textural properties and "mouthfeel". Suitable agents include natural gum binders such as gum tragacanth, xanthan gum, gum karaya and gum arabic, seaweed derivatives such as Irish moss and alginates, smectite clays such as bentonite or hectorite, carboxyvinyl polymers and water-soluble cellulose derivatives such as hydroxyethyl  
25 cellulose and sodium carboxymethyl cellulose. Improved texture may also be achieved, for example, by including colloidal magnesium aluminium silicate. Suitably, the structuring agent is included in an amount from up to about 5%, preferably up to about 3% by weight of the oral hygiene composition.

Fluoride sources suitable for use in all oral hygiene compositions of the present invention include sodium fluoride, zinc fluoride, potassium fluoride, aluminium fluoride, lithium fluoride, sodium monofluorophosphate, stannous fluoride, ammonium fluoride, ammonium bifluoride and amine  
5 fluoride.

Preferably, the fluoride source is present in an amount sufficient to provide from about 50 ppm to about 4,000 ppm fluoride ions in the composition. Inclusion of a fluoride source is beneficial, since fluoride ions are known to become incorporated into the hydroxyapatite of tooth enamel,  
10 thereby increasing the resistance of the enamel to decay. Fluoride is also now thought to act locally on the tooth enamel, altering the remineralisation-demineralisation balance in favour of remineralisation. Inclusion of a fluoride source is also desirable when a polyphosphate anti-calculus agent is included, in order to inhibit the enzymic hydrolysis of  
15 such polyphosphates by salivary phosphatase enzymes.

Suitable desensitising agents include, for example, formaldehyde, potassium nitrate, tripotassium citrate, potassium chloride and strontium chloride (suitably as hexahydrate), strontium acetate (suitably as hemihydrate) and sodium citrate.

20 Flavouring agents may be added to increase palatability and may include, for example, menthol, oils of peppermint, spearmint, wintergreen, sassafras and clove. Sweetening agents may also be used, and these include D-tryptophan, saccharin, dextrose, aspartame, levulose, acesulfam, dihydrochalcones and sodium cyclamate. Typically, such flavouring agents  
25 are included in amounts up to about 5%, preferably up to about 2% by weight of the oral hygiene composition. Colouring agents and pigments may be added to improve the visual appeal of the composition. Suitable colourants include dyes, such as FD & C blue No.1, D & C yellow No.10

and D & C yellow No.3. A suitable and commonly used pigment is pigment grade titanium dioxide, which provides a strong white colour.

Suitably, as described above, the compositions of the invention may include a further antimicrobial agent as a preservative and/or anti-plaque agent. Suitable antimicrobial agents include zinc salts (such as zinc citrate), cetyl pyridinium chloride, the bis-biguanides (such as chlorhexidine), aliphatic amines, bromochloro-phene, hexachlorophene, salicylanilides, quaternary ammonium compounds and triclosan. Enzymic systems providing a source of a natural biocide may be used as alternatives to or in combination with the biocides listed. For example, a system comprising lactoperoxidase and glucose oxidase may be used to generate antimicrobial amounts of hydrogen peroxide in the presence of glucose, water and oxygen.

The composition may also comprise an anti-calculus agent. Suitable anti-calculus agents include zinc salts such as zinc citrate and zinc chloride and poly-phosphates. Suitable pyrophosphates include the sodium and potassium pyrophosphates, preferably disodium pyrophosphate, dipotassium pyrophosphate, tetrasodium pyrophosphate and tetrapotassium pyrophosphate. A preferred source of pyrophosphate is a mixture of tetrasodium pyrophosphate and tetrapotassium pyrophosphate.

It will be appreciated that when choosing components from the lists above, the components chosen must be chemically and physically compatible with one another.

Particularly suitable oral compositions are those in the form of a toothpaste or liquid dentifrice. A liquid dentifrice contains components commonly associated with a paste eg abrasives, humectants and actives,

but the viscosity is considerably lower, and is preferably below about 50,000 cps.

According to another aspect of the present invention, there is provided a method of cleaning the buccal cavity for cosmetic purposes by  
5 oral application of any oral hygiene composition as defined above. As used herein the term "buccal cavity" denotes inter alia the mouth, the teeth and the gums.

In a further aspect, the present invention provides a method of treating and/or preventing dental caries and/or gingivitis by oral application  
10 of any oral hygiene composition as defined above.

In yet a further aspect of the present invention, there is provided the use of a composition as defined above in the treatment and/or prevention of dental caries and/or gingivitis.

In a still further aspect of the present invention, there is provided  
15 the use of a composition as defined above in the manufacture of a medicament for the treatment and/or prevention of dental caries and/or gingivitis.

The nature of the present invention is illustrated by the following Examples, which should not be considered to limit the scope of the  
20 present invention in any way.

Example 1

A toothwhitening toothpaste was prepared to the following composition:

<u>Component</u>	<u>Concentration (% w/w)</u>
5 Non-crystalline sorbitol (70% in aqueous solution)	50
Silica thickener (available under the trade name "Sident 22S")	10
10 Silica abrasive (available under the trade name "Sident 9")	8
Cellulose abrasive (available from Degussa AG under the trade name "Elcema P050")	2
15 Sodium lauryl sulphate, (available under the trade name "Empicol LZ PDR")	1.5
Sodium carboxymethylcellulose	0.9
Sodium fluoride BP	0.33
Titanium dioxide PH EUR	0.75
Sodium saccharin BP	0.26
20 Flavour	1 (by volume)
Sodium citrate BP	2.5
Purified water BP	22.7

Method of Formulation

The sodium fluoride, sodium saccharin, sodium citrate were  
 25 dissolved in purified water and the sorbitol solution was added. The silica abrasive, silica thickener, cellulose abrasive, sodium carboxymethylcellulose and titanium dioxide were added to the above

mixture and stirred under vacuum until the mixture was homogeneous. Then the sodium lauryl sulphate and flavour ingredient were added to this mixture which was stirred again under vacuum until homogeneous. The resultant toothpaste showed excellent cleaning properties in use.

## 5 Example 2

A toothwhitening toothpaste was prepared to the following composition:

	<u>Component</u>	<u>Concentration (% w/w)</u>
10	Non-crystalline sorbitol (70% in aqueous solution)	50
	Silica thickener (available under the trade name "Sident 22S")	10
15	Cellulose abrasive (available from Degussa AG under the trade name "Elcema P050")	5
	Silica abrasive (available under the trade name "Sident 9")	5
20	Sodium lauryl sulphate (available under the trade name "Empicol LZ PDR")	1.5
	Sodium carboxymethylcellulose	0.9
25	Sodium fluoride BP	0.33
	Titanium dioxide PH EUR	0.75
	Sodium saccharin BP	0.26
	Flavour	1 (by volume)
	Sodium citrate BP	2.5
	Monosodium phosphate BP	0.5
	Disodium phosphate BP	0.5
	Purified water BP	qs



Method of Formulation

The sodium fluoride, sodium saccharin, sodium citrate, monosodium phosphate and disodium phosphate were dissolved in purified water and the sorbitol solution was added. The silica abrasive, silica thickener, cellulose abrasive, sodium carboxymethylcellulose and titanium dioxide were added to the above mixture, which was stirred under vacuum until it was homogeneous. Then the sodium lauryl sulphate and flavour ingredient were added to the mixture which was stirred again under vacuum until homogeneous. The resultant toothpaste showed excellent cleaning properties in use.

Example 3

<u>Component</u>	<u>Concentration (% w/w)</u>
Non-crystalline sorbitol (70% in aqueous solution)	50.00
15 Silica thickener (available under the trade name "Sident 22S")	10.00
Cellulose abrasive (available from Degussa under the trade name "Elcema P050")	5.00
Silica abrasive (available under the trade name "Sident 9")	5.00
20 Sodium lauryl sulphate (available under the trade name "Empicol LZ PDR")	1.50
Sodium carboxymethylcellulose	0.90
Sodium fluoride BP	0.33
25 Titanium dioxide PH EUR	0.75
Sodium saccharin BP	0.26
Flavour	1.00 (By volume)

Sodium citrate BP	2.50
Sodium bicarbonate BP	5.00
Purified water BP	qs

#### Method of Formulation

- 5        The sodium fluoride, sodium saccharin, sodium citrate, sodium bicarbonate were dissolved in purified water and the sorbitol solution was added. The silica abrasive, silica thickener, cellulose abrasive, sodium carboxymethylcellulose and titanium dioxide were added to the above mixture, which was stirred under vacuum until homogeneous. Then the
- 10    sodium lauryl sulphate and flavour ingredient were added to the mixture, which was stirred again under vacuum until homogeneous. The resultant toothpaste showed excellent cleaning properties in use.

#### Example 4

	<u>Component</u>	<u>Concentration (% w/w)</u>
15	Non-crystalline sorbitol (70% in solution)	45
	Silica thickener (available under the trade name "Sident 22S")	9.5
	Cellulose abrasive (from Degussa under the trade name "Elcema P050")	5
20	Silica abrasive (available under the trade name "Sident 9")	5
	Sodium lauryl sulphate (available under the trade name "Empicol LZ PDR")	1.5
25	Sodium carboxymethylcellulose	0.7
	Sodium fluoride BP	0.33

	Titanium dioxide PH EUR	0.75
	Sodium saccharin BP	0.26
	Tripotassium citrate BP	2.5
	Potassium nitrate	5
5	Anhydrous trisodium phosphate	2
	Toothpaste flavour	1
	Purified water BP	21.46

#### Method of formulation

The sodium fluoride, sodium saccharin, tripotassium citrate, potassium nitrate and trisodium phosphate were dissolved in water which was heated to 45°C and the sorbitol solution was added. The silica thickener, silica abrasive, cellulose abrasive, titanium dioxide, sodium carboxymethyl cellulose and sodium lauryl sulphate were mixed together and added to the aqueous phase under vacuum. The resultant mixture was stirred under vacuum until the sodium carboxymethyl cellulose was fully hydrated and the mixture was homogenous. The flavour ingredient was added and the mixture stirred again under vacuum until homogenous. The resultant toothpaste showed excellent cleaning properties in use.

#### Example 5

20	<u>Component</u>	<u>Concentration (% w/w)</u>
	Non-crystalline sorbitol (70% in aqueous solution)	45
	Silica thickener (available under the tradename "Sident 22S")	7.5
25	Cellulose abrasive (from Degussa under the trade name "Elcema P050")	5

	Silica abrasive (available under the trade name "Sident 8")	5
	Silica abrasive (available under the trade name "Sident 10")	2
5	Sodium lauryl sulphate (available under the trade name "Empicol LZ PDR")	1.5
	Sodium carboxymethylcellulose	0.6
	Sodium fluoride BP	0.24
	Sodium saccharin BP crystalline	0.26
10	Titanium dioxide PH EUR	0.75
	Tetrapotassium pyrophosphate	2.77
	Tetrasodium pyrophosphate	2.77
	EDTA tetrasodium salt	0.2
	Toothpaste flavour	1
15	Monosodium phosphate	0.50
	Disodium phosphate	0.50
	Purified water	24.41

#### Method of Formulation

The sodium fluoride, sodium saccharin, tetrapotassium  
 20 pyrophosphate, tetrasodium pyrophosphate, EDTA tetrasodium salt,  
 monosodium phosphate and disodium phosphate were dissolved in water  
 and the sorbitol solution was added. The silica thickener, silica abrasives,  
 cellulose abrasive, sodium carboxymethyl cellulose, titanium dioxide and  
 sodium lauryl sulphate were mixed together and added to the above  
 25 aqueous phase under vacuum. The resultant mixture was stirred under  
 vacuum until sodium carboxymethyl cellulose was fully hydrated and the  
 mixture was homogeneous. The flavour ingredient was added and the  
 mixture was stirred again until homogeneous. The resultant toothpaste  
 showed excellent cleaning properties in use.

Example 6

<u>Component</u>	<u>Concentration (% w/w)</u>
Non-crystalline sorbitol (70% in solution)	45
5 D-panthenol (pro-vitamin B5 - a soothing agent)	0.15
Hexetidine 99 (antibacterial agent)	0.1
Cellulose abrasive (available from Degussa under the trade name "Elcema P050")	12
Titanium Dioxide PH EUR	0.9
10 Hydroxycellulose (a gelling agent available under the trade name "Natrastol 250 G")	4
Sodium monofluorophosphate	0.84
Sodium saccharin	0.26
Allantoin BCP'34 (a soothing agent)	0.15
15 Cocoamido propyl betain (a surfactant)	4.5
Toothpaste flavour	1 (by volume)
Colour	0.001
Purified Water BP	31.099

Method of formulation

- 20 The sodium monofluorophosphate, sodium saccharin, allantoin and D-panthenol were dissolved in purified water and the sorbitol solution was added. The cellulose abrasive, titanium dioxide and the hydroxycellulose were mixed together and added to the aqueous phase under vacuum. The resultant mixture was stirred under vacuum until hydroxycellulose was
- 25 fully hydrated and the mixture was homogeneous. The colour, flavour, hexetidine and cocoamido propyl betain ingredients were added to the mixture, which was stirred again under vacuum until homogeneous. The resultant toothpaste showed excellent cleaning properties in use.

Example 7

<u>Component</u>	<u>Concentration (% w/w)</u>
Non-crystalline sorbitol (70% in aqueous solution)	45
5 Sodium saccharin BP crystalline	0.26
Sodium monofluorophosphate	0.84
Sodium carboxymethylcellulose	0.85
Silica abrasive (available under the trade name "Zeodent 163")	12.22
10 Silica abrasive (available under the trade name "Zeodent 113")	6
Cellulose abrasive (available from Degussa under the trade name "Elcema P0500")	4
Zinc citrate trihydrate	0.5
15 Titanium dioxide PH EUR	0.75
Sodium lauryl sulphate	1.75
Sodium bicarbonate	2
Bromochlorophene	0.1
Toothpaste flavour	0.939
20 Purified water	25.041

Method of Formulation

The sodium monofluorophosphate, sodium saccharin and sodium bicarbonate were dissolved in water and the sorbitol solution was added. The toothpaste silica thickener, toothpaste silica abrasive, cellulose  
 25 abrasive, titanium dioxide, zinc citrate, trihydrate, sodium lauryl sulphate and sodium carboxymethylcellulose were mixed together and added to the aqueous phase under vacuum. The resultant mixture was stirred under vacuum until the sodium carboxymethylcellulose had fully hydrated and the

mixture was homogeneous. The bromochlorophene was dissolved in the flavour ingredient and added to the previous mixture which was then stirred again until homogeneous. The resultant toothpaste showed excellent cleaning properties in use.

Claims

1. An oral hygiene composition comprising a combination of a particulate cellulose cleaning/polishing agent having a particle size of less than 50  $\mu\text{m}$  and a particulate non-cellulose abrasive.
- 5 2. An oral hygiene composition as claimed in claim 1, in which the cellulose has a particle size of less than about 40  $\mu\text{m}$ .
3. An oral hygiene composition as claimed in either claim 1 or 2, in which the cellulose comprises powdered cellulose.
4. An oral hygiene composition as claimed in any preceding claim, in  
10 which the non-cellulose abrasive comprises silica.
5. An oral hygiene composition as claimed in any preceding claim, in which the non-cellulose abrasive has a particle size of between about 25  $\mu\text{m}$  and about 45  $\mu\text{m}$ .
6. An oral hygiene composition as claimed in any preceding claim  
15 which further comprises an agent to provide enhanced cleaning action selected from: alkali metal bicarbonate, alkali metal orthophosphate, alkali metal citrate and any compatible mixtures thereof.
7. An oral hygiene composition comprising a particulate cellulose  
20 cleaning/polishing agent and an agent to provide enhanced cleaning action selected from: alkali metal bicarbonate alkali metal orthophosphate, alkali metal citrate and any compatible mixtures thereof.



8. An oral hygiene composition as claimed in either claim 6 or 7, in which the agent to provide enhanced cleaning action is selected from: sodium bicarbonate, trisodium orthophosphate and tripotassium citrate.
- 5 9. An oral hygiene composition as claimed in claim 7, in which the cellulose is the sole abrasive ingredient.
- 10 10. The use of an oral hygiene composition as claimed in any preceding claim, to remove stains from teeth and/or to reduce and/or prevent build-up of stains on teeth.
- 10 11. The use of an oral hygiene composition comprising a particulate cellulose cleaning/polishing agent as the sole abrasive ingredient, to remove stains from teeth and/or to reduce and/or prevent build-up of stains on teeth.
- 15 12. The use of an agent to enhance cleaning/polishing action of an oral hygiene composition, the agent being selected from: alkali metal bicarbonate, alkali metal orthophosphate, alkali metal citrate and any compatible mixtures thereof.
- 20 13. A method of cleaning the buccal cavity for cosmetic purposes comprising oral application of an oral hygiene composition as claimed in any of claims 1 to 9, or the use of an oral hygiene composition, as claimed in any of claims 10 to 12.
14. A method of treating and/or preventing dental caries and/or gingivitis by oral application of an oral hygiene composition as claimed in any of claims 1 to 9.

15. The use of an oral hygiene composition as claimed in any of claims 1 to 9, in the treatment and/or prevention of dental caries and/or gingivitis.
  16. The use of an oral hygiene composition as claimed in any of claims 1 to 9, in the manufacture of a medicament for the treatment and/or prevention of dental caries and/or gingivitis.
- 5

# INTERNATIONAL SEARCH REPORT

International / Publication No  
PCT/EP 95/02308

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 6 A61K7/16

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP,A,0 480 172 (DEGUSSA AG) 15 April 1992 cited in the application see the whole document & US,A,5 158 764 ---	1,3-5, 10,13-16
A	US,A,3 146 170 (BATTISTA) 25 July 1964 see the whole document ---	1-16
A	DE,A,14 44 311 (FMC CORPORATION) 31 July 1969 see the whole document ---	1-16
A	FR,A,2 625 676 (LABORATOIRES PHARMASCIENCES) 13 July 1989 cited in the application see the whole document ---	1-16
-/--		

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents :

- \* "A" document defining the general state of the art which is not considered to be of particular relevance
- \* "E" earlier document but published on or after the international filing date
- \* "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \* "O" document referring to an oral disclosure, use, exhibition or other means
- \* "P" document published prior to the international filing date but later than the priority date claimed

- \* "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \* "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \* "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \* "&" document member of the same patent family

Date of the actual completion of the international search

6 November 1995

Date of mailing of the international search report

21.11.95

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentaan 2  
NL - 2280 HV Rijswijk  
Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl,  
Fax (+ 31-70) 340-3016

Authorized officer

Fischer, J.P.

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/EP 95/02308

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DE,A,28 16 513 (VEB ELBE-CHEMIE) 26 October 1978 see the whole document ---	1-16
A	DE,A,29 22 671 (BATTELLE-INSTITUT) 4 December 1980 see the whole document ---	1-16
A	PATENT ABSTRACTS OF JAPAN vol. 4 no. 151 (C-28) [633] & JP,A,55 098111 (LION HAMIGAKI) see abstract & CHEMICAL ABSTRACTS, vol. 93, no. 22, 1 December 1980 Columbus, Ohio, US; abstract no. 210119s, see abstract ---	7,9-11, 13-16
A	FR,A,493 389 (SLAIGHT) 7 August 1919  see the whole document ---	7,9-11, 13-16
A	CHEMICAL ABSTRACTS, vol. 99, no. 26, 26 December 1983 Columbus, Ohio, US; abstract no. 218412b, see abstract & TR. NAUCHNOISLED KHIM-FARM. INST., vol. 13, 1983 pages 171-178, ---	7,9-11, 13-16
A	CHEMICAL ABSTRACTS, vol. 98, no. 12, 21 March 1983 Columbus, Ohio, US; abstract no. 95486y, see abstract & TR. NAUCHNOISLED KHIM-FARM INST., vol. 12, 1982 pages 181-186, -----	7,9-11, 13-16

1

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 95/02308

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP-A-480172	15-04-92	DE-A- 4113044 BG-A- 95283 DE-D- 59100507 ES-T- 2060263 US-A- 5158764	21-05-92 24-03-94 25-11-93 16-11-94 27-10-92
US-A-3146170	25-08-64	NONE	
DE-A-1444311	31-07-69	CH-A- 432550 FR-A- 1363884 NL-A- 284076	30-09-64
FR-A-2625676	13-07-89	NONE	
DE-A-2816513	26-10-78	NONE	
DE-A-2922671	04-12-80	NONE	
FR-A-493389		NONE	

Form PCT/ISA/210 (patent family annex) (July 1992)